SUPPLEMENT TO

THE MEDICAL JOURNAL OF AUSTRALIA

Number 6, January 9, 1943.

WAR MEDICINE AND SURGERY

Compiled under the direction of the Committee on the Survey of War Medicine of the National Health and Medical Research Council.

THE SUPPLY AND USE OF BLOOD AND BLOOD SUBSTITUTES.

It is probable that, during this year, blood will be collected from some two to three million donors in America alone. This enormous figure gives an indication of the importance now attached to the use of blood and blood derivatives in medicine and surgery. A large literature on the subject has grown up, and from this the following topics have been chosen because of their general interest: (*a*) the supply of human blood; (*b*) the grouping of blood; (*c*) complications of blood transfusion; and (*d*) blood derivatives and substitutes.

Supply of Human Blood.

It has never been seriously claimed that there was a better all-round source of human blood than the healthy, adult donor; but, at various times, cadaver blood and placental blood have been looked on as useful supplements to this supply. Cadaver blood, from those who die a violent death, has the unexplained but useful property of reliquefying within about one hour of the death. If the corpse is then placed in the high Trendelenburg position, some two litres of blood can be aseptically removed from the internal jugular vein. This blood is considered safe if taken within eight hours of death, and has proved effective therapeutically. It cannot, however, be widely available, even in times of war, and its collection would run counter to public sentiment in English-speaking countries. Even stronger arguments than these can be brought against the use of placental blood. The yield from each placenta averages less than one hundred cubic centimetres, and the rate of contamination is dangerously high.

It is usually accepted that the withdrawal of 500 cubic centimetres of blood has little harmful effect on the health of properly selected donors, provided there is a reasonable time between donations. When one considers the relatively few studies made of the regeneration of blood after hæmorrhage, and the disagreement between such results as have been obtained, it is obvious that the reasonable interval between donations cannot yet be accurately defined. The blood volume begins to increase immediately after hæmorrhage, and is back to normal in forty-eight to seventy-two hours. This restoration, however, is due to an increase in plasma volume. In the first two hours the fluid added is poor in protein; but the volume does not reach the normal figure until the body has replaced the plasma protein, possibly from the liver.

The regeneration of hæmoglobin takes much longer. One group of workers[2] found that, after the removal of about 550 cubic centimetres of blood, the average time for recovery of normal hæmoglobin value was fifty days. The time required was shorter in men than in women, and did not increase with successive donations. It is important to note, however, that 25% of the subjects studied needed over sixty days to complete regeneration. This is one instance in which the spread of the results, as well as the average value, has to be considered. Thus, if the time interval between bleedings of 550 cubic centimetres were fixed at sixty days, it would be ten days greater than the average time required, but would still be too short for one-quarter of the donors. Another public health consideration is that nowadays repeated venesections are being made on members of a population which is subject to a wartime diet. It has even been suggested that blood donors should be given iron preparations as a routine procedure. This has proved successful in the case of professional donors; but, applied to large numbers of voluntary donors, it would help to solve one problem at the risk of creating others, for it would be costly to the transfusion service, and somewhat unpleasant to the subjects.

The Grouping of Blood.

The widespread use that has been made of universal donor blood probably indicates that the average doctor does not want the responsibility of blood grouping. His hesitation is well founded, for, although in the vast majority of cases blood grouping is a simple procedure, there are occasional pitfalls, and even an occasional mistake is serious. In 1939 large numbers of people were hurriedly grouped in England. Subsequent examination showed that as many as 10% from some districts had been wrongly grouped.

Because of the importance of blood grouping, an investigation of the available methods has been carried out by the Medical Research Council in Britain, and a reliable technique has been described.[3] The usual methods are subject to certain errors. Impotent serum is the commonest cause of difficulty; for sera of the same group contain agglutinin in different amounts, and only the high-titred sera will give reliable results. Active serum is especially important in testing for Groups A and AB. These groups are subdivided into A_1 and A_2, in the case of the former, and A_1B and A_2B in the case of the latter. Cells containing A_2 factor, particularly those in A_2B group, are very weak in agglutinogen and will not agglutinate with low-titre serum. Serum which is strong against A_1 cells is usually relatively strong against A_2 as well, but this is not necessarily so. Therefore, the anti-A test serum must be tried against a known A_2B blood and shown to agglutinate it.

In other cases false positive reactions are seen. Testing serum that is not carefully prepared is liable to contain non-specific agglutinins which act at low temperatures ("cold agglutination"). Bacterial contamination of the serum or the cell suspension also tends to cause agglutination. The formation of rouleaux may be mistaken for agglutination (pseudo-agglutination). Further errors are introduced by clerical mistakes.

In order to eliminate all these errors the following three measures have been recommended: (*a*) The serum should be examined for agglutinins as well as the cells for agglutinogens; this checks both technical and clerical errors. (*b*) The examination should be made with small test tubes rather than by a slide method, since test tubes give fewer false positive reactions. (*c*) Doubtful or negative samples, as examined macroscopically, should be checked with the microscope.

In the vast majority of cases the results of examination of the cells and of the serum will be concordant; for example, specimens of blood with A in the cells will have β-agglutinin in the plasma, and so on. Where agreement is not shown, a reexamination is made. Very occasionally, it is found that an expected agglutinin cannot be demonstrated in the serum. These "defective blood groups" are rare, but do occur.

A final test is made in order to avoid the danger of grouping A_2B as B. All samples of blood which are apparently Group B are subject to a further examination, in which the serum is tested against A_2 cells. A_2B blood can never contain an agglutinin which reacts with A_2 cells, otherwise it would show auto-agglutination. B blood, however, always contains an α-agglutinin which reacts with A_2 cells. Therefore, in this distinguishing test, the serum from Group B blood gives agglutination, and that from Group A_2B does not.

A knowledge of the various agglutinins is useful in studying some of the rarer hæmolytic agglutination reactions. The relevant facts in regard to the iso-agglutinins may therefore be described briefly. The α-agglutinin occurs normally in all B and O blood; it reacts with A_1, A_2, A_1B and A_2B cells. The α_1-agglutinin also occurs normally in all B and O blood and abnormally in A_2 and A_2B bloods; it reacts with A_2 and A_1B cells. The α_2-agglutinin is rare, occurring occasionally in A_1 and A_1B; it reacts with A_2 and A_2B cells and also, strangely enough, with O cells. The β-agglutinin, of course, is present in O, A_1 and A_2 blood and reacts with B, A_1B and A_2B cells.

Complications of Blood Transfusion.

The complications of blood transfusion[6] are: (*a*) incompatibility; (*b*) transfusion of contaminated blood; (*c*) pyrexial reactions; (*d*) transmission of disease; (*e*) circulatory embarrassment.

Incompatibility.

Errors in blood grouping should be very rare if the proper technique is used. They do seem to occur, however, even in the best hospitals. Wiener reports two cases that occurred amongst three thousand transfusions, in spite of a careful routine of grouping the serum and cells of both donor and recipient, and of cross-matching their blood. In the first case there was an accidental exchange of samples; in the second, auto-agglutination of the donor's blood was mistaken for true agglutination. The commonest error, however, is a failure to detect the A_2 factor, and this has led to several hæmolytic reactions, since subgroup A_2 makes up 20% of Group A. Protection against these major errors of incompatibility is threefold. The first is the grouping test; the second is the cross-matching test, in which the donor's corpuscles are tested with the recipient's serum; and the third is the biological test, in which the first twenty to fifty cubic centimetres of the transfusion are run in slowly, and signs of a reaction are looked for, before the bulk of the transfusion is given.

The universal donor (Group O), once used freely so as to avoid blood grouping, has been employed less and less of recent years. His plasma contains α-agglutinin and β-agglutinin, so that a reaction may be expected, theoretically, whenever O blood is given to Groups A, B, or AB. It has always been assumed, however, that the danger from the transfusion of incompatible plasma is relatively slight. Dilution occurs rapidly and some of the agglutinin is absorbed by the plasma and vessel wall, which contain, in small quantities, the same agglutinogen as the red blood cells. Severe reactions are therefore improbable, except in the case of those Group O donors whose agglutinins are of a high titre, and these people have been termed "dangerous universal donors". Some recent work has clarified the position regarding such donors.[6] A certain number with agglutinins of very high titre were chosen and transfusions of their serum or plasma were deliberately given. In no case did a dangerous reaction occur, but, in every recipient, some red cell destruction could be demonstrated, and symptoms were caused in a proportion of them. It is therefore unwise to use these donors for transfusions when the patient requires chiefly red blood cells; but, if the main indication is to restore blood volume, the universal donor may be freely used, with no more precautions than the standard cross-matching and biological tests. The A and B factors can now be obtained in pure chemical form and some successful trials have been made of adding these to universal donor blood so as to reduce the agglutinin titre.

There are a number of cases in which incompatibility has been present, even though the grouping was correct and the universal donor was not to blame. These are cases of intragroup incompatibility. They are not often due to incompatibility between the subgroups A_1 and A_2 or A_1B and A_2B. Reaction between these types of blood will occur only when the α_1-agglutinin or α_2-agglutinin is present in them. The α_2-agglutinin is especially rare, but, since it agglutinates O cells as well as A_2 cells, it is potentially more dangerous. When these agglutinins do occur, they are of low potency and are usually active only at low temperatures. It is suggested, however, that if the irregular agglutinin is present at all, its titre may be increased considerably, as an immune response, whenever the incompatible agglutinogen is transfused. An initial transfusion of A_1 to A_2 blood or *vice versa* is therefore almost always safe, but a second transfusion is much more to be feared.

The blood groups are divided into various types according as the agglutinogens M, N and P are present or absent. These agglutinogens are safely ignored in transfusion work, because the corresponding agglutinins do not normally occur in human serum, and are not produced as a response to transfusion. The risk from type incompatibility is negligible.

By far the most frequent cause of intragroup incompatibility is the interaction between Rh agglutinogen and anti-Rh agglutinin. The Rh agglutinogen is found in 85% of the population. The remaining 15% lack this factor and a small proportion of them may form an antibody against it if transfused with "Rh-positive" blood. An "Rh-negative" pregnant woman can also develop anti-Rh agglutinin as a result of the antigenic stimulus of an "Rh-positive" fœtus.

For repeated transfusions it is therefore best to have an "Rh-negative" donor. The same applies when a transfusion is to be given to a pregnant or puerperal patient. Theoretically, it might be expected to apply to any "Rh-negative" person who has ever received a transfusion from an "Rh-positive" donor and to any "Rh-negative" woman who has borne an "Rh-positive" child. The anti-Rh agglutinin, however, usually disappears from the blood stream fairly rapidly after the stimulating agglutinogen has been removed. An occasional exception to this might be expected, and has been reported.

Unfortunately, the antiserum for Rh testing is not yet available for routine work. Incompatibility can sometimes be detected by the cross-matching test, provided certain precautions are taken. The agglutinin is usually most active at low temperatures, and, therefore, when a transfusion is to be given to a pregnant or puerperal woman, or to someone who has recently received a transfusion, a special cross-matching test is done with cooled reagents. This test is not extremely reliable, and in these cases the biological reaction, which is the last line of defence, must be carefully observed. It is also a commonsense precaution that any transfusion should be discontinued immediately unusual symptoms occur.

A rare cause of hæmolytic reaction is cold agglutination, which can occur only if the blood is given very cold. It can be detected by the cross-matching test, and avoided by warming the blood.

The effects of an incompatible blood transfusion are included under the general name of hæmolytic reaction,

ILLUSTRATIONS TO THE SYMPOSIUM ON LYMPHOGRANULOMA INGUINALE BY DR. H. F. BETTINGER, DR. F. M. McDONALD AND DR. H. H. JOHNSON.

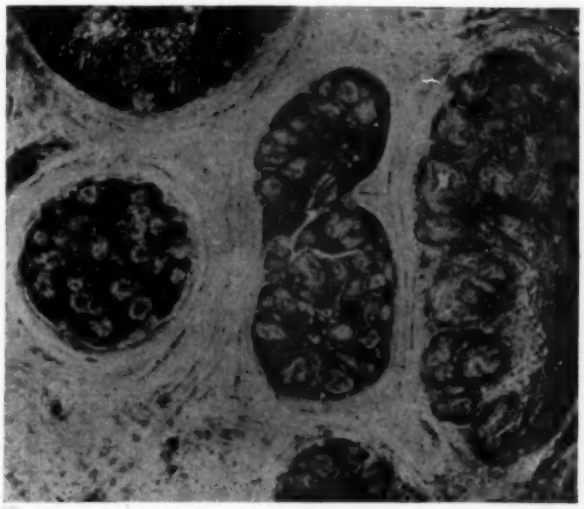

FIGURE V.
Low power photomicrograph of a group of inguinal lymph glands showing the periadenitis and the numerous micro-abscesses in the glands.

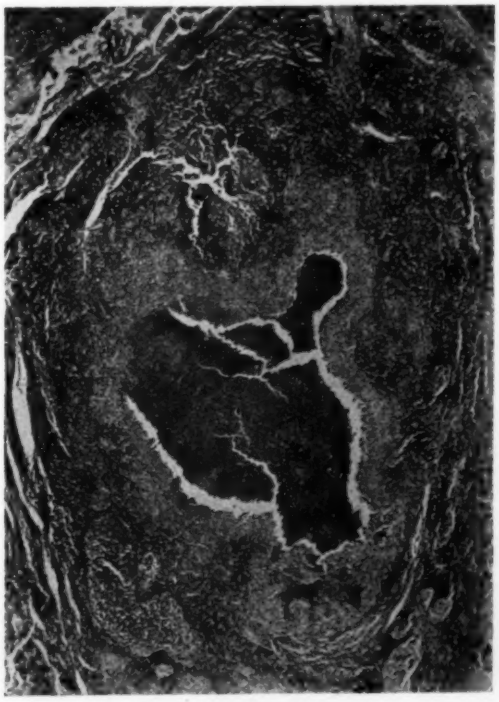

FIGURE VI.
One of the abscesses under higher magnification. The centre consists of polymorphonuclear cells and debris. The pale zone of epithelioid cells surrounding the centre can be well distinguished from the adjacent lymphatic tissue.

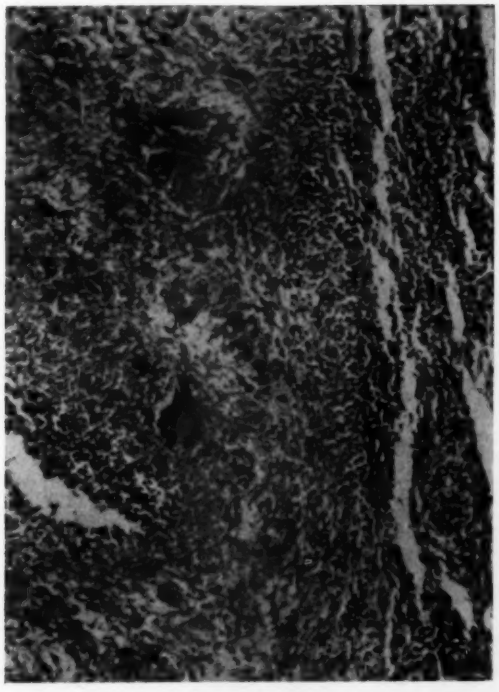

FIGURE VII.
The centre of the abscess is just seen at the left lower margin of the picture. In the zone of epithelioid cells a Langhans giant cell is included. The surrounding lymphatic tissue is seen at the right of the picture.

ILLUSTRATIONS TO THE SYMPOSIUM ON LYMPHOGRANULOMA INGUINALE BY DR. H. F. BETTINGER, DR. F. M. McDONALD AND DR. H. H. JOHNSON.

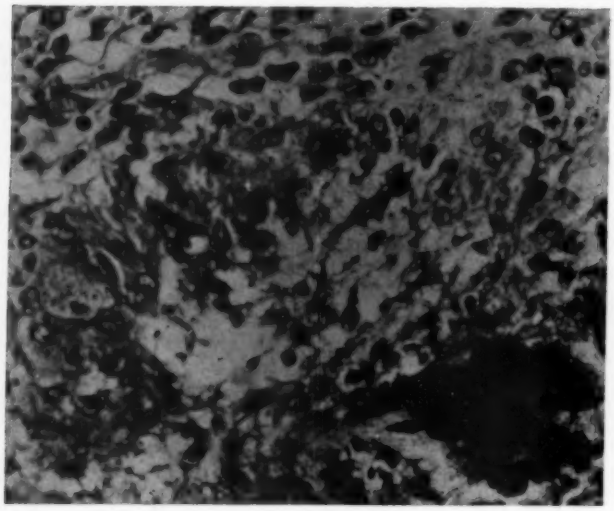

FIGURE VIII.
High power view of the epithelioid cell zone.

FIGURE IX.
Stellate micro-abscesses in the Fallopian tube.

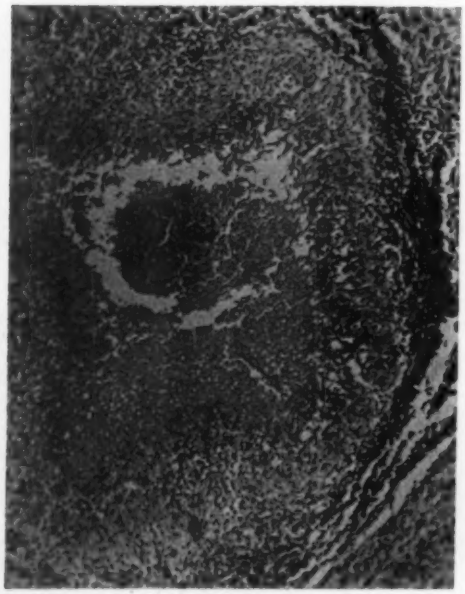

FIGURE X.
Details of one of the abscesses, clearly showing the palisade arrangement of the epithelioid cells at the edge of the central area of necrosis.

FIGURE XI.
Positive response to the Frei test.

since agglutination is usually the prelude to hæmolysis. Hæmolysis can occur independently of agglutination, however, and this is another reason for performing cross-matching tests in test tubes rather than on slides.

A hæmolytic reaction is not necessarily fatal, even when large amounts of incompatible blood have been transfused. When death does occur it is due to renal failure, which may sometimes be caused by mechanical blocking of the uriniferous tubes with precipitated acid hæmatin. Such precipitate is not formed in every fatal case, however. The early signs and symptoms of an incompatible transfusion are suffusion of the face, restlessness and anxiety, violent pain in the back and respiratory embarrassment. Later there may be rigors, circulatory collapse, hæmoglobinuria, hæmalbuminæmia, jaundice and symptoms of embolism. The patient may apparently recover and then develop renal failure. In the mildest form of hæmolytic reaction little or nothing may be noticed, except that the transfusion is ineffective.

A problem sometimes arises in distinguishing a reaction due to incompatibility from the more violent of the non-specific reactions. These latter are more common and much less serious. A useful differentiating symptom is the characteristic lumbar pain of the true hæmolytic reaction, possibly due to spasm of the renal artery. If incompatibility is suspected, the transfusion is stopped, the grouping and cross-matching are repeated, the patient's blood is examined for bilirubin and free hæmoglobin, and the urine is tested for hæmoglobin. The patient's blood used to recheck the cross-matching test should be blood drawn before the transfusion began, since the first effect of an incompatible transfusion is the absorption of the patient's agglutinin by the transfused cells. Later, the foreign cells stimulate the patient to produce very high agglutinin titres and an examination of his serum five to ten days after the transfusion readily shows it to be incompatible with a sample of the same blood as that transfused.

The treatment of a hæmolytic reaction is to make the urine alkaline, to give abundant fluids, especially glucose solution, and to give a small transfusion of absolutely compatible blood. This last measure sometimes causes dramatic relief of the lumbar pain. Alkalinization of the urine is best carried out by giving intravenously ten cubic centimetres of twice molar sodium lactate solution and ten cubic centimetres of a saturated solution of sodium bicarbonate. The urine becomes alkaline in fifteen minutes and remains so for at least one and a half hours.

Transfusion of Contaminated Blood.

Bacterial contamination of blood occurs in spite of a careful aseptic routine. The inoculum of bacteria is small and, if the blood is administered fresh, or even in most cases if it is stored properly, no reaction to it occurs. The blood may become highly dangerous, however, if it is allowed to stand at room temperature for even a few hours.

Pyrexial Reactions.

A slight rise in temperature soon after a blood transfusion is very common. Some authors do not even classify it as a reaction, and therein lies part of the difficulty of determining the rate of reaction obtained by different workers. Definite rigors should not occur in many more than 1% of transfusions.

The commonest cause of a non-specific reaction is the injection of certain foreign material, given the general name of pyrogen. It is important to realize that non-pathogenic bacteria can produce pyrogens, and that these substances are not destroyed by autoclaving. Thorough cleaning will remove pyrogens, but if the cleaned material is not immediately sterilized pyrogens will return, for there are numerous air-borne bacteria that can multiply even in distilled water. If scrupulous attention is paid to cleanliness, and if apparatus is not exposed to the air for long periods prior to autoclaving, a very satisfying reduction in the rate of reactions can be produced. In the classical work which demonstrated the importance of pyrogens in blood transfusion, the reaction rate was reduced from 12% to 1·2%.

Transmission of Disease.

There are many diseases which the donor has occasionally transmitted to a recipient through blood transfusion. They include influenza, measles, typhoid, septicæmia, encephalitis, smallpox and rickettsial diseases. The three commonest, however, are syphilis, malaria and allergic conditions.

By 1939 there had been reported 68 cases of transfusion syphilis, and many unreported cases had undoubtedly occurred. The incubation period shown was one to four months, and the disease usually appeared in the form of secondary lesions. The spirochætes of syphilis are killed when blood is stored for four days or longer at 2° to 4° C. or when plasma or serum is desiccated. It is customary to do a serological test for syphilis on blood donors, but its usefulness is limited. By the time an infected person gives a positive reaction to this test, the spirochætes have usually disappeared from the blood stream.

Transfusion malaria, in a high percentage of cases, is transmitted by people who are unaware that they have the disease. Great stress must therefore be placed on an inquiry to ascertain, not only whether the donor has had malaria, but also whether he has lived in a malarious district. Examination of blood smears is not reliable as a way of excluding the disease. One donor who transmitted malaria had had no symptoms of the complaint for forty years. The gift of blood may reactivate a quiescent malaria in the donor himself, possibly because the parasites are present in the blood reservoirs. The parasites can withstand low temperatures, and malaria has been transmitted by stored blood.

The danger of transmission of allergic disease is small if blood or plasma is pooled. When an allergic reaction occurs during or soon after the transfusion, it is explained as a sensitivity of the patient to some food recently taken by the donor, or to some normal constituent of the donor's blood. There have also been cases of the passive transfer of a donor's sensitivity. In one definite case the patient had a sensitivity to strawberries for three months after receiving blood from a sensitive donor. It is because of such cases that transfusion from a donor with a history of allergic complaints is not recommended.

Circulatory Embarrassment.

The danger of circulatory embarrassment and pulmonary œdema is ever present in the transfusions of peace time. It is not so great a danger when the patient is one who, prior to wounding, was in good health. Small people, however, are likely to be given too large a transfusion if they are given standard amounts. The same applies to old patients. In any case, whenever more than two pints have to be given rapidly, a careful watch should be kept on the lung bases.

Blood Derivatives and Substitutes.

Stored Blood.

Fresh blood is obviously the ideal therapeutic form of blood, but large quantities cannot be quickly obtained. Blood stored at 2° to 4° C. is an excellent substitute. Various changes take place during storage, such as decrease in leucocytes, complement and prothrombin. These changes are of theoretical importance if the blood is to be used in the treatment of certain medical conditions; but they seem insignificant if the blood is required for the treatment of shock. The objection to the use of whole blood in severe burns associated with hæmoconcentration has probably been over-emphasized. If the blood volume is maintained, hæmoconcentration is tolerated well. The non-specific reaction rate for stored blood is, strangely enough, rather less than for fresh blood.

The longer the blood is stored, the shorter is the life of the red blood cells after transfusion; but the safe period for storage varies with the preservative used. If glucose is added to the preserving fluid so that the final concentration in the blood is 0·25% to 0·5%, the blood cells are of quite good quality after at least two or three weeks. Although hæmolysis is currently accepted as an indication that the blood should no longer be used, it is doubtful whether the injection of a few grammes of hæmoglobin is harmful,

since up to twenty grammes have been given safely in experiments when the urine was made alkaline beforehand.

Bacterial contamination is a problem when stored blood is being used. Only a few of the infected specimens show obvious deterioration to the naked eye and all samples cannot be tested by culture methods. Therefore, the blood must be maintained at a low temperature (2° to 4° C.) during storage, and the biological test must be carefully observed. If the conditions for collecting the blood are good and the refrigerating plant is adequate, it is the general experience that stored blood is bacteriologically safe. It is probable, however, that a few bacteria get into as many as 10% of the samples during bleeding, and precautions must be strict to prevent them from multiplying.

In the absence of cold agglutination, the warming of blood prior to transfusion is unnecessary, time-consuming and possibly dangerous. It is very easy to over-heat the outside of the flask and so produce pyrogenic products. Another point in the giving of stored blood is that a filter must be used, since citrate is not a perfect anti-coagulant and small clots are often present.

Plasma.

Plasma is prepared by siphoning off the fluid after the corpuscles have been centrifuged down or have been allowed to settle. It can be prepared from stored blood which has not been used within the specified time, or from fresh blood specially drawn to be processed for its plasma. When prepared on a large scale it is always pooled, and this has the advantage of producing a low agglutinin titre, so that the plasma can be given to a patient of any blood group. It has been found that the final titre is not the average of the original titres, but that a reduction occurs after pooling. The probable reason for this reduction in titre is that the A and B specific substances are present in plasma as well as in red corpuscles, and therefore cross-absorption of agglutinins occurs in the mixed sample.

The citrate originally used as an anti-coagulant is siphoned off with the plasma, and therefore dilutes the final product. Sterility tests are done on all specimens. If it is true that blood is frequently contaminated during collection, then the plasma prepared from it will also be contaminated, especially as the siphoning and pooling add a further risk. The organisms may be dealt with in one of two ways. The commonest method is to add a preservative such as merthiolate or one of the sulphonamides. These, particularly the former, give good, but never complete, protection. The other method is to filter the plasma by means of a Seitz filter. This is difficult, because fibrinogen clogs the filter pads, and therefore most plasma is unfiltered.

Liquid plasma gradually develops clots, and also is a favourable medium for bacterial growth, so that there is a growing opinion that plasma should not be stored in the liquid state. It should be frozen solid and kept in that form, or else dried. Freezing and drying have different fields of application, and the best results are obtained by the use of both methods of preservation. The solid is prepared for use by quick thawing; slow thawing gives a cloudy solution. The dried plasma is reconstituted by the addition of sterile, pyrogen-free water. Dried plasma is the blood derivative selected for use by the armed services of America, and is therefore being produced on a large scale. No one nowadays doubts its value in shock, and many people believe it to be effective in the treatment of moderate hæmorrhage.

Serum.

A very efficient way of preparing serum is to draw blood into a small quantity of oxalate anti-coagulant, separate corpuscles and plasma in an Alfa-Laval separator, and then clot the plasma by means of calcium chloride. If the calcium chloride is added while the plasma is being rotated round a central rod, the clot can be made to wind compactly around the rod, and the yield of serum is very close to the theoretical maximum. Serum can also be prepared by drawing the blood into a vessel that has no anti-coagulant; but the yield in this case is very low. A further method is to clot plasma that has been siphoned off in the usual way from citrated blood. The citrate is used in some ten times the quantity of oxalate solution and so produces greater dilution of the final product. Serum runs readily through a Seitz filter and, in contradistinction to plasma, is almost always filtered. Filtration is a valuable safeguard against bacterial contamination.

Liquid serum is not so liable to bacterial growth as liquid plasma and, of course, it cannot clot. Nevertheless it, too, is frequently converted to dried serum, because the liquid in time develops a deposit which, to the naked eye, is indistinguishable from bacterial growth. It must be remembered that the drying of serum or plasma by present methods is an expensive process, and these products should not be preferred to whole blood when the latter is readily obtainable and therapeutically suitable.

The argument as to whether serum or plasma gives fewer reactions appears, in retrospect, rather partisan. The removal of fibrinogen from plasma in order to make serum does not seem to alter significantly the therapeutic value of the fluid.

Human Albumin.

Albumin can be separated from plasma by fractionation with alcohol at a low temperature. The preparation is cheaper and simpler than that of dried plasma. Albumin is more active osmotically than globulin and is more soluble. One hundred cubic centimetres of a 25% solution have as great an osmotic effect as about 400 cubic centimetres of plasma or 800 cubic centimetres of blood. This solution of albumin does not precipitate or become cloudy on standing unrefrigerated for many months. Preliminary clinical trials of human albumin in solution have so far been satisfactory. It raises the blood pressure rapidly, and may restart bleeding, so that great care is necessary in its use when concealed hæmorrhage is a complication. Albumin solutions are not the only blood derivatives with a high osmotic pressure, since dried serum or plasma may be reconstituted to three or four times their original strength, and so rival the albumin in this regard. Such concentrated serum and plasma have been used and found to give a high rate of reactions; the albumin solutions do not appear to do this.

Red Cell Suspensions.

The red cells separated in the preparation of plasma or serum are usually discarded. They can, however, be resuspended in a small amount of saline solution and used in certain anæmias in which plasma is unnecessary and sometimes undesirable. The rise in hæmoglobin value following transfusions of red cell suspensions is never as great as would be theoretically expected.

Blood Substitutes.

Gum acacia is now rarely used, because it is regarded as too toxic; but similar types of substitute, such as gelatin, isinglass and pectin, have been proposed. It is unlikely that they will be extensively tried while blood, which is obviously better, can be freely obtained from voluntary donors.

Crystalloid solutions such as normal saline solution, Ringer's fluid and glucose solution have their field of use, but do not compete with plasma or serum in the treatment of shock. Ascitic fluid has been used as a source of protein, but is available only in small quantities. An unsuccessful attempt was made to employ bovine plasma for intravenous therapy; it proved too toxic. Those engaged in this work, however, have now prepared bovine albumin, and claim that it is much less liable to give reactions than whole bovine plasma.

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